

## REMARKS

In the Office Action dated December 11, 2007, claims 1-22, 25 and 69-89 are pending and under consideration. Claims 1-22, 25 and 88-89 are allowed. Claim 82 is objected to as dependent from a rejected base claim (claim 81), but would be allowable if rewritten as an independent claim. Claims 69, 71-81 and 83-86 are rejected under §103(a) as obvious over Esenaliev (U.S. Patent 6,165,440) in view of Patel (US 2005/0180917 A1). Claim 70 is objected to under 37 C.F.R. §1.75 as a substantial duplicate of claim 1.

Claim 70 has been canceled by the foregoing amendment, rendering the objection thereof moot.

With respect to the obviousness rejection, it is believed that the Examiner may have intended to include claim 87 in the rejection, in addition to claims 69, 71-81 and 83-86. Applicants will address the rejection assuming that the rejection applies to claims 69, 71-81 and 83-87.

Initially, it is observed that independent claim 69 is written based on previous claim 23, which recites "0.1% metal by weight", wherein "0.1%" refers to the concentration of the metal "in said tissue or said population of cells in the animal". Claims 71-81 and 83-87 all depend from claim 69.

The Examiner alleges that Applicants fail to disclose adequate support for the limitations of previous claim 23 in Serial No. 09/363,204 filed on July 29, 1999, and therefore Patel is applied as prior art relative to claims 69, 71-81 and 83-87. The Examiner admits that Esenalieve fails to disclose a particular concentration of metal to be achieved within the tissue treated. However, the Examiner contends that Patel teaches the treatment of cancer at the site of, and area adjacent to, the tumor via irradiation of the diseased tissue. Referring to paragraph

0042 of Patel, the Examiner alleges that Patel teaches nanoparticles comprising a metal, such as gold, at a concentration of about 0.1% by weight. Therefore, the Examiner concludes that it would have been obvious to incorporate a metal concentration as suggested by Patel, to the composition of a nanoparticle as taught by Esenalieve, such that the susceptibility of a tumor to radiation is enhanced.

Applicants respectfully submit that the Examiner raised a rejection based on the combination of Esenaliev and Patel in a previous Office Action, which Applicants believe to have overcome based on distinguishing the references, independent of claiming priority from Serial No. 09/363,204.

Applicants reassert in this response that the Examiner's understanding of Patel's disclosure is incorrect. Patel is focused entirely on neutron capture therapy and therefore any material used for this must contain elements that have reasonable neutron capture cross sections, namely the isotopes listed by Patel:  $^{10}\text{B}$ ,  $^6\text{Li}$ ,  $^{22}\text{Na}$ ,  $^{22}\text{Co}$ ,  $^{123}\text{Co}$ ,  $^{126}\text{I}$ ,  $^{135}\text{Xe}$ ,  $^{148m}\text{Pm}$ ,  $^{149}\text{Sm}$ ,  $^{153}\text{Eu}$ ,  $^{155}\text{Gd}$ ,  $^{157}\text{Gd}$ , .....(See Paragraph [0036]). It is these isotopes that provide the potential therapeutic effect upon bombardment with thermal neutrons. These isotopes may be in the form of micro or nanoparticles. Patel also discloses that the nanoparticles containing the active isotope(s) listed above may also contain small amounts of additional metals, such as V, Mn,...gold (Au) .....(See Paragraph [0042]). These elements have very low neutron capture cross sections and are not useful for neutron capture therapy. The purpose or benefit of including these bystander elements with the neutron capture isotopes is not discussed in Patel. However, it is the concentration of these metals in the nanoparticles that Patel is referring to, i.e., these additional metals can be present in the nanoparticle "at a concentration of about 0.0001% wt/wt to about 0.1% wt/wt" .....(See Paragraph [0042]). This percentage clearly

refers to the concentration of the metal elements in the nanoparticles (composed mainly of active neutron absorbers), not the percentage of nanoparticles in the target tissue as recited in the present claims.

Accordingly, it is respectfully submitted that the rejection of 69, 71-81 and 83-86 under 35 U.S.C. §103(a) as allegedly obvious in view of Esenaliev in combination with Patel is improper. Withdrawal of the rejection is respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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